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A DISCUSSION OF THE USE OF BLOOD AND PLASMA TRANSFUSION*

Method of Influencing pH and Prothrombin of Plasma Intra-Marrow Injection of Concentrated Plasma in Shock

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Since the first authenticated transfusion was performed in 1667 the procedure has at times been in great favor but more often maligned and frequently discarded as of no therapeutic value. Certain men are outstanding in the history of its development, namely: William Harvey, James Blundell, Landsteiner, Crile, Agote, Lewisohn, Lindeman, and Unger.

With the advent of the use of citrate and certain apparatus for the administration of undiluted blood, surgical procedures were discarded and transfusions were used more widely. The discussion of whether citrated blood or whole undiluted blood was more advantageous continued for many years. As a matter of fact, the question is still undecided.

For the administration of whole blood the modified Unger apparatus, the Scannell, the Soresi, and the Debaka all prove satisfactory. For general hospital use, however, in which many people, seldom trained, are giving transfusions, reactions with the unmodified blood method are frequent and often severe. The citrate method seems preferable. Many times, too, because of technical difficulties, the patient does not receive the much needed blood.

BLOOD STORAGE

The citrate method at present enjoys wide usage as a result of increase in our knowledge of adequate blood storage.

The technique of collecting the blood is as follows: 50 cc. of 4% sodium citrate is placed in a liter flask under vacuum. The flask has rather thin, long neck so that it may be rotated more easily while blood is being obtained. We believe that considerable injury is caused to certain cell elements in extracting blood from the donor under a high degree of negative pressure. By citrating the tube and needle this is overcome in part. We collect most of our blood with little or no negative pressure. If large numbers of samples must be taken in a short period of time, the use of increased negative pressure permits the collection more quickly. Citrating the donor's tube is managed by inserting the donor's needle into the transfusion bottle, inverting it and thus the tubing and needle gradually fill with the citrate solution.

Specimens of blood are collected in two test tubes, one for serology and the other for use in typing and cross matching. Blood is stored in a specially made refrigerator, the motor of which is outside, thus eliminating vibration. There is an automatic control and alarm signal which operates whenever the temperature varies from 4 to 6 degrees C. The bottles are carefully checked and labelled. We keep the blood, usually, three and not more than four days. Blood that is not used is set aside for conversion into plasma.

The following changes have been reported as taking place in stored blood. The white blood cells are diminished in three to four days. Scudder states that the hemoglobin content remains fairly constant, from fifteen to twenty-five percent being found in the plasma. The mean cell diameter of the erythrocytes is reduced about twenty percent in thirty days and that the polymorphonuclear leukocytes are diminished by fifty percent in 48 hours and are amorphous masses in fifteen days but that lymphocytes, mono-

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cytes and eosinophils do not disintegrate so rapidly. Thrombocytes fall rapidly to a low level and then remain constant at about 30,000 for some fifteen days. We find the prothrombin is reduced but in blood that is kept no longer than three or four days the reduction is insignificant. Kolmer states that complement is well preserved for the first seven to ten days. Bacteriacidal activity of the plasma for bacillus typhosus is well preserved for seven days following which rapid deterioration occurs.

Scudder also states that blood sugar and hydrogen ion concentration are reduced within the first week. He feels that the shape of the flask in which the blood is stored is of considerable importance in reducing red cell and chemical change. By decreasing the interspace between plasma and cells at the point of the narrowest constriction one increases the interfacial potential. The cells on settling in this flask form the interface between plasma and cells at the point of the narrowest constriction. This type of flask may be of considerable value in the smaller hospital where there is a small turnover and the blood must be kept for longer periods. Under these conditions, glucose should be added to the citrate solution.

Maizes and Whittaker recommend a preservative as follows: sodium chloride .43 gms., sodium citrate (dehydric) 1.05 gms., dextrin 8.5 gms., distilled water 100 cc. Forty cc. of this solution are added to eighty cc. of blood.

If the blood is collected and stored under perfect conditions, using a glucose-citrate mixture, it is stated that the sample may be used with safety up to thirty days. This applies particularly to groups AB and B, which are at times difficult to obtain. I believe, however, that these samples, even though stored and under the most ideal conditions with the glucose-citrate mixture for long periods, are not as reaction proof as those stored only the recommended three to four days.

From the standpoint of safety it is probably better to eliminate blood that has been stored longer than ten days. Even in an active transfusion service it is sometimes difficult to keep specimens of Groups AB and B available for emergencies. We suggest that some of the AB and B blood be put up in the glucose-citrate mixture, carefully marked, and kept for a ten-day period.

As is well known, approximately 30,000,000,000 red blood cells break down during the course of twenty-four hours in the average person who lives at atmospheric pressure. Undoubtedly, this rate of breakdown continues when blood is outside of the body and it is logical to assume that many red blood cells constantly and physiologically break down during the storage of blood in an ice box. It is also well known that the glucose levels of stored blood drop rapidly from 100 mg. % to 0 mg. % in three or four days. This rapid decrease in the glucose is probably due to the continued activity of the white blood cells and to the action of the oxidizing enzymes normally present in the blood.

Because of the short storage period, we have not noted marked variations in percentage of hemoglobin (in mg. %), in the plasma of blood collected as described above. In other words the sudden reduction in pressure from that of one atmosphere to 20 inches of vacuum apparently does not rupture many of the red blood cells and the addition of glucose apparently does not alter significantly the rate of hemolysis during the storage period of four to seven days. After the blood has stood for that time, regardless of the method of collection and storing, the hemoglobin content varies from 110 to 260 mg. %.

PLAN FOR SMALLER COMMUNITIES AND HOSPITALS

In small transfusion units and in small hospitals the use of unmodified blood by a trained operator is satisfactory. Citrated blood for immediate use may be recommended. This blood should be filtered through two layers of sterile gauze before it is administered or run through a filter in the set. The question of plasma may be settled in one or three ways—dried plasma may be purchased from a pharmaceutical house and stored for emergencies or Strumia's method of freezing fresh plasma and keeping it frozen might be considered. Liquid plasma, ½ N. or isotonic, to which saline, glucose and merthiolate have been added, may be kept for long periods of time in the ice box (4 degrees C.) or even at

room temperature. With this latter procedure, of course, comes the problem of having facilities for freezing and for keeping the plasma frozen. The most satisfactory method, therefore, is to have dried plasma always on hand. An additional suggestion is that some one hospital centrally located be equipped and manned to supply blood and plasma to a given district. Each hospital in this district should be responsible for a percentage of the expense.

REACTIONS:

Using whole blood in 1,000 transfusions personally performed the percentage of reaction was 2.1%. In our Transfusion-Plasma Unit the reaction percentage in 1,000 citrate transfusions was 4.2% and during this past month it has been lowered to 2.1%. Mt. Sinai Hospital reports a reaction percentage between 5 and 6%.

A serious reaction, often fatal, occurs in some patients with acid urine. Acid hematin is precipitated in the renal tubules, suppression of urine and uremic symptoms occur. This may be prevented by alkalinization of the urine before transfusion in some cases.

Careful cleansing of the apparatus and rubber tubing is essential in prevention of reactions. Triple distilled water free of pyrogens should be used in preparing citrate solutions, in intravenous solutions and in cleaning tubing and apparatus.

Whenever high fever is present, the transfusion should be given at the low point of the temperature curve, if possible.

Another cause for reactions is the giving of RH positive blood to RH negative patients. The RH factor is an agglutinin present in the red cells of rhesus monkeys and in the red cells of about 85% of human beings. If an RH positive father marries an RH negative mother, his blood should not be used for transfusion for her even though the blood groups were compatible Landsteiner groups but a compatible RH negative donor must be obtained for a necessary transfusion. It is further suggested that the foetus may inherit certain dominant agglutinable substances from the father, which are lacking in the mother, and may stimulate the production of isoantibodies. The agglutinin in the mother's blood may penetrate the placental barrier so that the antibodies, by continued action on the blood cells of the foetus, may induce erythroblastosis fatalis and certain types of jaundice. In the presence of a sufficient concentration of agglutinins, the foetus may die in utero. It is important, therefore, to consider these possibilities in all parturient and abortion patients who are about to receive transfusion. An RH negative mother should be transfused with RH negative blood. Plasma may be used until such a donor is obtained.

In certain hemorrhagic states and in the treatment of acute and chronic infections, whole unmodified blood, when available and may be administered efficiently may be preferable.

PLASMA

Experimentally, plasma was used in 1871 by Bowditch and in 1872 by Luciana. Ward in 1918 set forth the advantages of concentrated plasma over whole blood in the use of emergencies at clearing stations.

Strumia was one of the first, if not the first, to use plasma and serum extensively. By 1931 he used concentrated plasma routinely.

There are many methods of preparing plasma. One—the ½ normal or normal plasma following the work of Elliott. Hill states that dilute or ½ normal plasma suffers from deficiencies seen following the use of saline and glucose solution in some instances. The crystalloid containing portions of these solutions may be lost in the tissues. The possible effectiveness of this procedure he does not deny and feels that its greatest value is in the most severe grades of dehydration. It may be of value, too, when added to the concentrated plasma treatment, in such conditions as nephrosis. We have some data to support the contention that normal liquid plasma is more effective in controlling the phenomena of hemophilia than is four or five times concentrated plasma.

Strumia freezes the plasma immediately after separation, adding merthiolate. Before this plasma is used, it must be liquified. This requires from 17 to 21 minutes. This, I think, is one of the real disadvantages as far as the treatment of shock is concerned for the immediate instillation of plasma is of the utmost importance many times.

Methods for drying plasma have been set forth by Flosdorff and Mudd, by Hartman, by Hill and others. The Adtevac method of Hill is the one used in our Transfusion-Plasma Unit. With this method mass production of four or five times concentrated plasma is conveniently accomplished. The dehydration is brought about by absorption in silica gel.

The technique is as follows: blood is collected in vacuum-type bottles. It is then either pooled at once and the plasma separated or it is placed in the bank until outdated (3 days), when it is then pooled to remove agglutinins. Two DeLaval separators arranged in series produce a yield of plasma of from 50 to 60%. Centrifugation results in a clear product with most of the fat removed. It is frozen immediately in carbon dioxide snow, placed in the machine and dehydrated or kept frozen in a special refrigerator until ready for dehydration. Gases and moisture are removed. It is possible to produce a product which contains considerably less than .03% moisture. The end product is broken up, placed in amounts from 12.5 gms. to 25 gms. in a rubber stoppered bottle in which a vacuum is induced and sealed with collodion. For each 12.5—16 gms., of material, a bottle containing 45 cc. of pyrogen-free distilled water is provided. A 50 cc. syringe is needed and a 19 to 21 gauge needle.

The water is drawn from the bottle and injected into the bottle containing the plasma. This is then shaken until the plasma is dissolved and ready for use—a step which takes about 30 seconds.

The material is light amber or slightly tinged with hemoglobin. Hemoglobin is present in amounts varying from 40 to 100 mgs.% Fibrinogen is present. The complement is not affected. The prothrombin content is reduced but it has been found that in patients with low percentage of prothrombin it can be given with the knowledge that it will increase the prothrombin fully as satisfactorily as frozen liquid plasma. The antibody content is not altered. Protein content averages 20 mg. %. It is possible to make this five times concentrated plasma or two times concentrated by the amount of pyrogen-free water that is added to a given amount of plasma.

DETERMINATION OF pH AND PROTHROMBIN LEVELS UNDER VARIOUS CONDITIONS

500 cc. of blood was withdrawn from four individuals—250 cc. of each of these bottles of citrated blood were transferred to other bottles containing 125 cc. of 10% glucose. These bottles stood in the refrigerator for three days and then were pooled and centrifuged. The plasma was aspirated. The blood without the glucose was likewise treated. The pH of the liquid plasma, containing glucose, was 7.6 and that without glucose was 7.55. The prothrombin in both was 43% of normal. The hemoglobin in mg. percent was 112 with glucose and 142 without glucose. Both sets of figures were corrected for dilution by determining the total nitrogen mgs. per 100 cc. of plasma. With glucose it was 567 mg. and without glucose 1,053 mg. The difference in pH levels, prothrombin percentage and hemoglobin content in fluid plasma with or without glucose was inconsequential. After the plasma was dried and then restored to its original volume by distilled water, the pH of the plasma with glucose was 7.9 and without glucose was 9.4. This would seem to indicate that the glucose prevented the release of the volatile products of the plasma. The prothrombin time of restored plasma with glucose was 5% and without glucose 14%. However, when the pH of each sample of plasma was brought to its original level before drying (i.e. 7.55 and 7.6 respectively), prothrombin time of the plasma, without glucose was 56% normal and with glucose 15% of normal. These findings are difficult of interpretation and require further study.

Many determinations have been made of prothrombin levels of restored plasma, the pH of which was brought to its pre-dried level. Invariably the prothrombin levels approximate those found in the pre-dried fluid state. This would seem to indicate that drying has no effect on the prothrombin levels of plasma, providing the pH is unaltered.

It is well known that the charge of plasma is positive and that of many blood substitutes is negative. Those, negatively charged, administered intravenously are probably re-

sponsible for the increased blood sedimentation rate.

Plasma preserved by the method described and treated with a carbonic acid solution, which restores the pH to the original predried level, could be very slightly, if at all, altered from its original state.

THE USE OF PLASMA

In our experience with several hundred injections of plasma made by the Adtevac method, unfavorable reaction occurred in only one patient. This was due to citrate sensitivity and was only a mild, febrile reaction.

There is considerable experimental evidence supporting plasma therapy in burns, wound healing, liver damage, massive exudations, intestinal obstruction, starvation, increased intracranial pressure, edemas and shock. Clinical evidence of the value of this material in these and in other conditions is mounting rapidly.

Indications for plasma transfusions are as follows:

1. Shock—traumatic, chemical, thermal.
2. Shock—associated with acute coronary occlusion.
3. Shock—with hemorrhage.
4. Dehydration—from diarrhea.
5. Hemorrhage—(plasma may be given before blood is available).
6. Infection—general or local in which there is loss of protein through the kidneys and protein intake from food is not sufficient.
7. Burns—loss of protein and fluids by exudation.
8. Nephritis—with marked albuminuria without edema when the plasma protein is not maintained at a satisfactory level.
9. Nephritis—with edema with marked hypoproteinemia and albuminuria.
10. Nutritional edema.
11. Hypoproteinemia—due to an inadequate protein intake.
12. Liver damage.
13. To promote wound healing.
14. Increased intracranial pressure.
15. Some cases of pulmonary edema which are refractory to bleeding alone.

Contraindications are few:

1. Congestive heart failure unless bled first.
2. Dehydration approaching a critical level of 6% of body weight. This may not be a valid objection.

In the treatment of these various conditions, methods for determining the state of hemoconcentration are often of great value. The following methods may be used:

1. Specific gravity—falling drop method.
   A more rapid fall indicates diminishing blood density which may be interpreted as a shift of fluid into the peripheral vascular channels. Since the increase in peripheral concentration usually precedes a fall in blood pressure it may be possible at times to determine impending shock by this method so that preventive measures may be used. (Scudder).
2. Red Blood Cell Count.
   A rise in the peripheral red cell count has been reported frequently. It has been stated that the greater the disproportion between the venous and peripheral blood, the graver the prognosis. Hemoconcentration is a characteristic of several types of shock, notably burns, marked dehydration, and certain chemical poisons, such as phosgene.
3. Hematocrit.
   The relation between the normal cell mass and serum content is 45-55. Changes in this relationship in either direction may aid in diagnosis and treatment.
4. Blood Volume.
   If there was a satisfactory, simple method to estimate total blood volume it would be of great help in determining the results obtained by various other methods. The Congo red and Evans blue are the ones most frequently used.

Irrespective of what theory of shock one accepts, everyone believes the amount of blood available for return to the heart is reduced, the size of the intracapillary bed is increased, the capillaries become more permeable, there is anoxemia and that the earlier treatment is instituted the better.

In the treatment of the shock syndrome it is important that aid reach the patient at once. This is particularly true in military service and is also true in maternity patients.

It is possible to prepare this four times concentrated plasma for injection and give it to the patient within 3 minutes. The product which we are making at present is dissolved in about 30 seconds. The average dose required to combat shock is 100 cc. In a few instances it may be necessary to give as much as 200-600 cc.

INTRA-MARROW ADMINISTRATION

Tocantins has shown that there is direct communication between the marrow and the general circulation. Materials injected into the marrow appear rapidly in the general circulation. This observation is of importance in the present discussion. Citrated blood, liquid plasma and concentrated plasma may be given by this route. At times veins are not available because of excessive fat, collapse, convulsions, extensive burns, in babies, or because of continued, unnatural motion, as aboard ship during a battle. In military use, concentrated plasma may be injected by syringe, intramarrowly, using a 16-20 gauge needle as rapidly as by the intravenous route. On the battlefield in mobile units, ambulances, on deck before transference to sick bay, shock may be given early treatment without recourse to the location of veins, removing clothing and the use of cumbersome bottles and tubing.

The main aim of shock therapy is to restore the circulating blood volume as quickly as possible thus breaking the anoxemic cycle and preventing increased capillary permeability and seepage of protein into the tissue spaces. When four times concentrated plasma is administered the patient usually responds very quickly and shows improvement in a matter of a few minutes. Normal or isotonic plasma may completely control shock by multiple infusion. Concentrated plasma rapidly increases the blood volume by withdrawing fluid from the tissues and stimulates the capillary non permeability through its hypertonicity.

If, after a five minute interval, a favorable response does not occur, the initial dose should be repeated. Hill reports that it was necessary to administer 600 cc. of four times concentrated plasma over a period of a few hours to control one case of shock. Shock may be prevented in certain special cases, particularly traumatic shock, by giving plasma before shock develops.

In treating burns with plasma it is essential to maintain the circulating plasma protein at a satisfactory level, particularly in the more severe burn cases. During the period of protein loss the maximum therapeutic efficiency can be obtained by a combination of normal and four times concentrated plasma. Hill has found that hemoconcentration was more effectively controlled when concentrated plasma was given along with normal plasma. In one of his cases, 6500 cc. of normal plasma and 1100 cc. of four times concentrated plasma plus glucose and saline were given over a four-day period. On the fifth day, a blood volume estimation with Evans blue revealed a normal plasma volume. Probably the optimum treatment for extensive burn cases is a combination form of treatment which includes normal plasma saline, glucose and concentrated plasma—the amount depending upon the individual results obtained from the tests for hemoconcentration and from the clinical course of the disease.

It has been shown that most surgical patients receive adequate fluids, carbohydrates, crystalloids and vitamins but frequently protein intake is not sufficient. This is particularly true in gastrointestinal operations. We have had a patient who suffered from a delayed ruptured appendix. He had peritonitis, liver involvement and deep jaundice. He was given the usual glucose-saline treatment. His blood protein diminished and the jaundice increased. He was given up as hopeless. Not until adequate concentrated plasma treatment was given did he improve, at which time his blood proteins, which had been 3.1, his carbon dioxide combining power which was 27, his N.P.N. which was 70, all began to approach normal figures. He received 550 cc. of concentrated plasma and his blood chemistry returned to normal and his jaundice was markedly lessened. This is an instance of the protective effect of the plasma protein on the liver and on the general blood chemical picture of the surgical patient. Similarly it is true that patients with congenital megacolon, jejunal fistula, chronic intestinal obstruction and other intestinal conditions can be kept in nitrogen balance by means of ade-

quate protein intravenous administration. The amount given depends upon the case. Intestinal and gastrointestinal anastamoses are often ineffective when the protein content of the blood diminishes. Such conditions can be remedied by adequate intravenous protein feeding.

Plasma is available in the treatment of nutritional edema. We have seen recently a patient with unexplained infection associated with a compound fracture of the femur. Unfortunately we saw him in the terminal stage when his edema was marked and his blood proteins were 3.2. In spite of what we thought was adequate intravenous protein therapy, he gave only a partial response as far as edema and the general condition was concerned. At post mortem it was found that he had, in addition to the conditions already mentioned, a pyonephrosis, an abscess of the prostate and, of course, pyuria. I believe that had we seen the patient earlier and used larger doses of plasma more frequently the blood picture would have improved.

At present we are treating a patient with subacute glomurelonephritis who has marked general body edema, hypoproteinemia (N.P.N., 70; creatinin, 5; cholesterol, 372; CO2, 27; and protein, 3.2) and an anemia. She has received 100 cc. concentrated plasma every other day, a total of 1000 cc. with 200 cc. heparinized plasma. Previous to this she has had all the well known diuretics without any appreciable effect. With the increased plasma intake she has recently put out 2500 cc. of urine which is twice as much as she has put out at any time in the last three months. Her blood proteins at present are 4.5 and specific gravity of the urine is 1.020 from a low of 1.006 and the albumin in the urine is reduced from plus 4 to plus 2. The edema is disappearing. Both normal plasma and four times concentrated plasma have been used. It would seem that use of the liquid and concentrated plasma is more satisfactory in this and similar conditions. Most of the results reported on the use of plasma in this condition have been disappointing. The concomitant anemia has been treated by two small transfusions (200 cc.), iron, liver extract (parenteral and by mouth), stomach extract. The high protein diet was not tolerated and had to be discontinued until lately.

In the treatment of dehydration, unless there has been a tremendous loss of body fluid as a result of extreme dehydration, the use of concentrated plasma to combat shock is indicated. It is also of great value in association with a hyperdermoclysis of saline in withdrawing the fluid more effectively into the circulation and at the same time lessening the capillary permeability.

Two patients with acute coronary occlusion developed shock reactions and were treated by us. They were first bled and then given ½ dose of four times concentrated plasma—i.e.: 6.25 gms. in 22.5 cc. of pyrogen-free distilled water. Both responded with an increase of blood pressure from 70 to 110, in one instance, and from 60 to 115, in the other instance, and both recovered without more shock symptoms

DISCUSSION

I think it is important that we should use plasma sensibly, with the thought that it may increase blood volume, and therefore we should prepare certain patients for this blood volume increase by bleeding, or we should anticipate the result of the plasma instillation by any method that we use ordinarily in the treatment of a given condition. From our experience we agree with Hill that the four times concentrated plasma is the optimum treatment for the conditions which we have mentioned. There is much to be learned concerning its use. As far as the preparation is concerned, I think we have answered most of the objections, and have added to the technique of Hill, i.e., by freezing the blood immediately after pooling or after filtration and separation in carbon dioxide snow. Since we have done this we have had no trouble with plasma clotting and have produced a product which has increased "flash solubility" so that we may get a soluble material in as little as 20 to 30 seconds after the addition of pyrogen-free distilled water. The addition of carbon dioxide increases the prothrombin percent and reduces the pH to normal.

CONCLUSIONS

1. A method for citrating and storing blood is discussed.
2. Reactions are less than 2.5%.

3. Suggestions for a small unit in a small hospital are made.
4. Indications for plasma are set forth.
5. Technique of making four times concentrated plasma is given.
6. A discussion of the use of the four times concentrated plasma, as compared with other plasma, is given.
7. The treatment of shock, burns, hypoproteinemia, and edema are discussed.
8. The addition of carbon dioxide to concentrated plasma increases the prothrombin percent and reduces the pH of the plasma to normal.
9. Intra-marrow injection of concentrated plasma is a signal advance in the treatment of war shock.
10. Intra-medullary infusion or transfusion may be used when veins are not available.

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DISCUSSION

DR. F. A. HEMSATH (Wilmington): I think our Scientific Committee should be congratulated upon their foresight in having this very timely subject presented at this Society meeting, and in securing the services of such an able essayist. I have enjoyed his presentation very much, and his very beautiful colored illustrations.

This subject is a very large one, and I think that the essayist, if he wished, could have taken up his entire time in the discussion of the historical development of the subject. I am limited to five minutes, which I do not want to use because we are behind in our program. I think that those who are working on this subject could get together and spend all of one day in discussing technique, so there is no use of our going into that. The entire subject of blood substitute for transfusion has been given a tremendous impetus again, of course, because of war conditions.

There has been, as he suggested, a division of thought by members of the Blood Transfusion Commission of the National Research Council, one advocating serum, another plasma, and still another one albumin from beef serum. The latter is not as radical as it seems because it is material that has been prepared even in a concentrated form. As I understand, however, it is antigenic, is it not?

DR. JONES: Yes, sir.

DR. HEMSATH: Other substitutes are still being studied and proposed and have not even passed the preliminary study. I think from a practical point of view we should realize now that plasma is here and available for your use, whether you are in a hospital or a medical center, or not. Whether you get the doctor's preparation of plasma, whether you buy Sharp & Dohme's, or whether you buy the preparation of any other company which may subsequently put it out, if you can obtain dried sterile plasma, you can carry it in your obstetrical bag, and you can use it at long distances from hospitals. You are not dependent on blood typing, and you undoubtedly will be able to save lives which have heretofore been lost because of the impossibility of getting the patient to the hospital for a transfusion.

I am very much interested in your remarks about the desirability of obtaining methods for blood volume studies, because in these days of large amounts of intravenous fluids of all kinds, it seems desirable at times to have some idea as to the blood volume of the patient, as the days go by in the treatment.

I wish to say again that I have enjoyed your presentation very much and I am sure we all have. Thank you.

DR. D. M. GAY (Wilmington): The transfusion with modern apparatus and with pro-

per control as to the production of hydrogen-free water is apparently a very safe procedure. Yet Dr. Jones touched upon some of the reactions which fortunately rarely occur under properly controlled conditions. However, the 2.7 per cent reactions that are reported may be serious, and in fact may be fatal, and it is of considerable importance as to what might be done to prevent these things.

Two things have come out in the literature within the last few years which lead me to ask Dr. Jones if it is practicable to test for the so-called rH factor, which apparently is the cause of some transfusion reactions, some even fatal reactions. Then one other thing which might be done to avoid certain percentages of reactions is apparently the alkalinization of the patient's urine to prevent the precipitation of hemoglobin when that is formed through the laking of the transfused blood. It has been shown that in transfusing dogs with dog hemoglobin, as long as their urine is alkaline the hemoglobin goes through without doing any apparent harm. However, immediately the urine becomes acid then there is a precipitation in the kidneys of some form of hemoglobin and the dogs frequently die.

Along this line I recall some work has been done by way of saving the 50 per cent or so of red cells which is ordinarily discarded in the preparation of plasma. It is my understanding that hemoglobin exerts an osmotic pressure five or more times that of the proteins in the plasma. Therefore, if we could only use this hemoglobin to increase the osmotic pressure of the plasma in these patients in shock and so forth it would be very useful to do so. It is to be hoped that further work along this line may perfect the use of hemoglobin as well as blood plasma.

I have one other question to ask Dr. Jones, and that is with relation to his statement that one should avoid giving any other intravenous medication just before a transfusion. I presume that he did not include in that the use of saline solution or glucose, because it is very common practice to use saline or glucose preceding or following blood. I would like clarification on that point.

Thank you.

DR. E. R. MILLER (Wilmington): I would like to ask a question of Dr. Jones about avoiding reactions of an allergic character. We know that supposedly these days about 10 or 15 per cent of all people are allergic, and I would like to know whether the allergic history is carefully gone into in regard to some of the reactions.

DR. E. G. LAIRD (Wilmington): I would like to know who manufactures those needles for bone marrow transfusion.

DR. G. J. BOINES (Wilmington): I would like to take a minute to say that I had the privilege of seeing the wonderful exhibit of Dr. Tocantin's last year at the AMA, where he illustrated and showed to us the method of sternal and bone marrow transfusion he was giving.

A month ago we had a case at Wilmington General, a girl eight years old, who bled profusely all day and half the night. This was postnasal bleeding. The child went into shock and we weren't able to get into the veins. We cut into the arms and the leg, and finally decided to give the transfusion in the sternum. We gave her 300 cc. of blood and 500 cc. of normal saline without any trouble, and the child made a good recovery. We wouldn't hesitate to use this method in children with septicemia when we are not able to get into the veins.

DR. JONES: I wish to thank these gentlemen for their very nice discussion. Regarding the rH factor, we haven't yet met up with any of these particular individuals. However, we are equipped to test for the rH negative and positive, and we hope we don't find any. It is strange that these things come up now, because in probably 15,000 transfusions that I did before the days of the blood storage methods, I don't remember any reaction that we might have had with transfusion of whole and modified blood that we could possibly have laid to one of these factors.

It is also said that agglutinins developed, anti-M and anti-N, as a result of repeated transfusions. Weiner, I think, believes that, but Rosenthal does not believe that that is possible. In almost any of these subjects that come up for discussion we can get more than one opinion, and that is particularly true

about this question of hemoglobin precipitating in the kidneys and producing anuria.

We never had that happen with whole blood. We have had such a reaction occasionally at Jefferson. I am not entirely sure as to the cause, and whether we can blame it altogether on whether or not there is an alkaline or acid urine. I do not think anybody can answer that question now. We never had a reaction of that type with whole blood, and yet that has been reported. One of the difficulties with this question of reaction is this: If you have not seen the blood given, if you do not know how it was given, you can not say definitely what the cause of that reaction might be. The fellow who is writing the article might know, but he is not going to tell, possibly. Many reactions happen with transfusions that are not due to any rH factor or anti-M and N, but are due to somebody's carelessness, and that is a pretty tough thing to work out.

We would like to be able to give them hemoglobin intravenously in quantities to make it valuable. I hope it can be worked out. Of course, we can use some of the fresh red cells, wash these red cells and put them in a crystalloid solution and give that, but it just seems too bad to waste all those good red cells that we collect in large quantities.

Regarding the saline administration before transfusion, I do not mean it should not be done, but if you can avoid it, do so, because reactions occur with saline administration. Sometimes one gets as high as one per cent of reactions, particularly if saline and glucose are given together, not so much with saline alone, as with saline and glucose. Even if pyrogen-free water is used and everything is done under the best possible technique, still reactions do occur with saline and glucose, or glucose alone, in one per cent of the cases.

We go into the allergic history of the patients, but I have not seen very many reactions with blood, as far as the patient is concerned. If the donor has had food very shortly before the blood is taken one might be able to transmit this reaction possibility to the patient. In fact, we have seen instances of urticaria develop. So we try to collect our blood from donors who are fasting, and that is not always possible, of course.

The needles can be obtained from Pilling. As far as septicemia is concerned, I do not see any particular reason, if we had to go into the bone marrow, why we should not in septicemia. The bone marrow circulation contains the infection just as the circulating blood does, because it is directly connected with the main bone marrow circulation.

TOXIN ANTITOXIN IMMUNIZATION AND INTRADERMAL IMMUNIZATION AGAINST SCARLET FEVER IN ADULTS*

GEORGE J. BOINES, M.D.**
Wilmington, Del.

Since the development and refinement of the methods of testing and immunizing the positive reactors, the incidence of diphtheria and scarlet fever among nurses has been practically eliminated in many general and communicable disease hospitals. The National League of Nursing Education requires that all applicants to a nursing school must be properly tested and immunized against the following diseases: small pox, diphtheria, scarlet fever and typhoid and paratyphoid fever. All the local hospitals, that is, Delaware, Memorial, Wilmington General and St. Francis, attempt to enforce these requirements. Before this work was undertaken, the method used in obtaining these tests and immunizations was left to the family physician of each applicant and the hospital did not check or re-check these tests when the applicants entered the hospitals and came in contact with patients. The hospitals did not enforce, on the other hand, that the positive reactors be properly immunized before being accepted into the nursing school.

Investigators have pointed out that the most reliable method of testing and immunizing is for this work to be done in the hospital in which the applicants enter. By doing this all the tests are made uniformly and the results can be kept under better control.

In Wilmington all the contagious cases are sent to the Doris Memorial Hospital, so that

*Read before the Medical Society of Delaware, Wilmington, October 8, 1941.

**Associate in Communicable Diseases, Wilmington General Hospital.

the general hospitals do not treat any diphtheria or scarlet fever. This lessens the number of contacts, except of course when patients with these infectious diseases are accidentally admitted for other conditions. This is not true of the nursing staff of the Doris Memorial who must take care of these infections. The nursing staff of this hospital is made up chiefly of affiliating nurses from the four city hospitals and the State Hospital. Heretofore, these affiliates were not tested before coming on duty.

In order to compare the incidence of these diseases among the Wilmington hospital nurses, the cases reported and treated at the Doris Memorial were studied. It was found that in the five-year period 1935-1939 there were five cases of tonsillar diphtheria and fifteen cases of scarlet fever. Two of the diphtheria and four of the scarlet fever cases were contracted while affiliating at the Doris Memorial. During these five years there were 145 cases of diphtheria and 387 cases of scarlet fever patients treated in this hospital. For this same period 307 student nurses affiliated and of this number two contracted diphtheria and four scarlet fever. While this number is apparently small, we must keep in mind that it represents a loss of several months in sick days. Most of the affiliating nurses are from the Wilmington General Hospital, each student spending two months there, while the other hospitals send their students for only one month.

The number of students trained in each hospital during 1935-1939 were: Delaware, 245; Memorial, 148; Wilmington General, 86; and St. Francis, 84; making a total of 563 for the four hospitals. Of these, 15 developed scarlet fever and five developed diphtheria. The total loss in hospital sick days was 331 days for the scarlet, and 75 for the diphtheria cases. Of course, all of these nurses were sent home for several weeks to convalesce, which is not included in the above time lost.

The reason for this survey is to show that the incidence of scarlet fever and diphtheria among nurses in hospitals where careful testing and immunization was carried out is much smaller than that in the Wilmington hospitals. In the Philadelphia Hospital for Contagious Diseases, where a large number of cases are admitted each year, not a single case of diphtheria and only one case of scarlet fever in an insufficiently immunized nurse occurred in the last three years (according to Dr. P. F. Lucchesi, Superintendent).

Hektoen and Johnson studied the value of immunization in the Durant Hospital, where scarlet fever and diphtheria cases only were admitted. Their observations establish that naturally Schick and Dick negative young women are well protected against diphtheria and scarlet fever. Further, that susceptible young women immunized to negative Schick and Dick tests before assuming active nursing of diphtheria and scarlet fever patients are also well protected.

METHOD OF IMMUNIZATION

DIPHTHERIA

In spite of antitoxin, diphtheria demands great respect and has involved absence from duty ranging from six weeks to twelve weeks per case. Thus, a very small number of cases can accumulate a great deal of loss in nurses' time.

In the past few years most of the large hospitals have made Schick testing and immunization compulsory. This requirement has practically eliminated diphtheria among nurses in these institutions.

This year we have tried to test and immunize all the susceptible reactors among the entire personnel, nurses and employees, at the Wilmington General Hospital; student and graduate nurses at the Delaware Hospital; the students of the State Hospital, and the Visiting Nurses of Wilmington. Each individual was tested by an intradermal injection of .1 cc of diphtheria toxin on the left forearm. Care was taken in each case to produce an intradermal wheal. The reading was made at 72 hours and the reaction was recorded in centimeters in its largest diameter. All reactions of one centimeter and over were read as positive. A control test was not deemed necessary, since pseudo-reactions usually fade out by the end of 72 hours.

All individuals with a positive reaction received a course of three subcutaneous injections of one cubic centimeter of toxin-antitoxin at weekly intervals given at the deltoid area. Two weeks after the last injection the Schick test was repeated and those found still

positive were given three additional injections, thus producing an active immunity to diphtheria in practically all individuals. Since the introduction of diphtheria toxoid for children, the use of toxin-antitoxin has more or less been put aside by many physicians, and toxoid was used to immunize the nurses. It has been found, however, that many adults do not tolerate toxoid and very painful local and general reactions resulted. It is now recommended that the use of toxoid be limited to children up to twelve years of age, and that the diphtheria toxin-antitoxin be used in all individuals over that age. Since this toxin-antitoxin is prepared from sheep's blood it reduces to a minimum the chance of subsequent inconvenience from reactions in case serums have to be given.

REACTIONS

Due to a hypersensitiveness to proteins there may be a redness and swelling at the site of injection and a general reaction with malaise and slight increase in temperature. The symptoms usually subside in 24 to 48 hours. None of our cases were made ill enough to go to bed or lose time from work.

A total of 344 individuals were tested, of whom 177 or 51% were positive. The size of reactions ranged from 1 to 10 cm., and several had a considerable central necrotic area. The number positive to the Schick test consisted of 50% of the graduates, 50% of the students and 57% of the personnel. Of the 177 Schick positives who received the three injections, 147 or 83% were negative two weeks after the last injection; the other 30 were rendered negative after receiving three additional injections.

SCARLET FEVER

Although immunization against scarlet fever has been adopted as a routine rule in many large hospitals and certainly all of the communicable disease institutions, one meets considerable opposition when this procedure is mentioned to many physicians. The principal drawback of the scarlet fever toxin has been the severity of the reactions that it occasionally produces. These reactions are never serious and greatly minimized if one takes the necessary precautions. The prevention of scarlet fever among student nurses by giving the Dick test to determine susceptibility and by the immunization of susceptibles has proven effective wherever used.

For the nine years included in a study by Anderson and Reinhardt, those hospitals that did not provide immunization had a scarlet fever incidence among their nursing staff over four times as great as was found in the immunized hospitals.

METHOD OF IMMUNIZATION

The method of immunization referred to by the workers mentioned was by the regular Dick method of five subcutaneous injections given at weekly intervals. The present doses are graduated as follows:

1st dose	650	skin test doses
2nd dose	2,500	" " "
3rd dose	10,000	" " "
4th dose	30,000	" " "
5th dose	100,000	" " "

The Dicks recommended that these doses be broken down into smaller ones according to the size of the reaction to the Dick test. This is done in order to avoid unnecessarily severe reactions in highly susceptible individuals.

In the past three years Dr. P. Lucchesi, of the Philadelphia Hospital for Contagious Diseases, has been using the intradermal method of immunization by employing 1/10cc (.1cc) of each of the five standard doses, that is, 1/10cc of the first dose or 65 skin test doses are injected intradermally on the surface of the forearm, this is followed at weekly intervals by 1/10cc of the second, third, fourth and fifth doses. If a severe reaction should occur in any individual then ½ of the following dose is given at the next injection and this is followed by the next regular dose.

The advantage of the intradermal method is that the reactions are not at all severe and only an occasional individual complains of a sore arm or a slight elevation of temperature. The intradermal method of immunization was employed in our work.

We tested 344 individuals, ranging in age from 19 to 45 years. Seventy-nine were graduate nurses, 205 student nurses, and 60 hospital personnel. The regulation Dick test was done on both forearms using 1/10cc of the scarlet fever toxin material. A control was not done since pseudo-reactions are not common. Before doing the tests several precau-

tions must be taken to insure uniform reactions. The arms were carefully washed with sterile sponges and sterile solutions as follows: soap, alcohol, water and dry sponge; the alcohol is washed by the sterile water to avoid any reactions of the alcohol with the toxin.

All syringes and needles were autoclaved in order to avoid the presence of water. The toxin vial was wiped with alcohol and dried with sterile sponge, then punctured with a sterile hypodermic needle. Several syringes were filled at one time so as to avoid multiple puncture of the vial and possible contamination. Regular toxin syringes with 1/10cc divisions were used.

Small special intradermal ¼-inch 26 or 27 gauge needles were employed, one needle being used for both arms of each case. The syringe was rinsed out with a small amount of the skin test solution before filling it for use after sterilization and each needle was rinsed out by ejecting 1/10cc of the skin test solution before making the test injection. Care was taken to produce a good sized wheal in the skin regardless of the amount used according to the graduations on the syringe, since at times some material leaked out of the needle or some air might be present in the syringe.

The tests were read between 20 and 24 hours and the reactions were measured in centimeters in their longest diameters. Regardless of the size of the test all were started with the same dose of 1/10cc intradermally at weekly intervals. Several had marked reactions with slight elevation of temperature and a few complained of nausea and headache. Ten grains of aspirin relieved most of the complaints. Of the entire group only three remained in bed overnight because of a slight temperature. No one had any infection; no anaphylactic reaction and no serum sickness was noted. Of the 344 tested, 130 or 37.5% were found positive to the Dick test; 113 or 87% of these were completely immunized by the intradermal method described. Two weeks after the last immunizing dose another Dick test was done using 1/10cc on the right forearm and 2/10cc on the left forearm, 96 or 85% were found entirely negative. The positive ones were given 1/10cc of the fifth dose over again and two weeks later retested. Only three were found still positive; of these, two had another 1/10cc of the fifth dose and were finally negative. The remaining one was allergic to the Dick test and to the control after she had received the five injections.

This work was done by testing groups of 20 to 40 at one time, starting about 7:30 in the morning so as not to inconvenience those working at night. One supervisor was in charge of the records and another for preparing the arms. Trays with the sterile syringes and needles were arranged on a table. The information obtained on the record included the name, hospital, age, weight, and history of diphtheria, scarlet fever, rheumatic fever, nephritis, and allergy. Those who ever had diphtheria or scarlet fever were found negative to the disease. One case with a rheumatic heart was positive to the Dick test but was not immunized because some of the workers fear the possibility of aggravating the disease.

Both the Dick and the Schick tests were done at the same time, one Dick test on each forearm and one Schick test on the left forearm. Those found positive to one or both tests were immunized by giving diphtheria toxin-antitoxin on Tuesday and the scarlet fever toxin on Friday of the same week.

All material used in our work was supplied by the Delaware State Board of Health.

By continuing to immunize all of the nurses and those who come in contact with scarlet fever cases, we hope to lessen the number of cases of scarlet fever among the nurses and at the same time protect patients and children from acquiring the disease from nurses who develop it while on duty. It is hoped that the intradermal method of immunization for scarlet fever will prove more encouraging as far as reactions are concerned and that it will be used more generally in all the institutions which handle children or whose nurses come in contact with contagious diseases. Since we began this work in September 1940 we have not had any diphtheria or scarlet fever among those immunized. There were, however, two cases of scarlet fever in two non-immunized nurses and one diphtheria in a non-immunized employee.

SUGGESTIONS

1. All students should have a Dick and Schick test done by the hospital as soon as they enter the Nursing School as preliminaries, and those found positive should be immunized by the method outlined above.

2. It is not necessary to require that a Dick and a Schick test be done by the family physician of the prospective student because it is not convenient for him to go to the trouble and expense necessary for only one test.

3. All immunizations should be done before the preliminary nurse comes in contact with patients, if possible.

4. Nurses who do not have the tests done or those who are positive to either test should not be permitted to affiliate at the hospital for contagious diseases.

5. All hospital attendants who come in contact with children or maternity patients should be tested and immunized if positive.

6. In order to avoid contamination and quarantine of children's wards by the accidental admission of contagious diseases, it is suggested that hospitals have an observation ward where all children should be placed on admission and kept for 48 hours before being moved to the large wards.

NUMBER IMMUNIZED IN 1940
Wilmington General Hospital

	No.	Neg.	%	Pos. Schick	%	Pos. Dick	%
Reg. N.	20	9	45%	8	40%	6	30%
Spec. N.	83	31	37.5%	40	48%	26	31%
Pers.	59	18	30.5%	34	58%	20	34%
	162	58	36%	82	50%	52	32%
Delaware Hospital							
Reg. N.	33	7	21%	16	49%	16	49%
Spec. N.	122	34	20%	63	51%	53	43%
Pers.	1	....	.....	....	.....	1	.....
	156	41	26%	79	51%	70	45%
Visiting Nurses							
Reg. N.	26	8	31%	16	61%	8	31%
Totals							
Reg. N.	79	24	30%	40	50%	30	35%
Spec. N.	205	65	32%	103	50%	79	39%
Pers.	60	18	30%	34	56%	21	35%
	344	107	31%	177	52%	130	38%

Of this group 70 were positive to both the Schick and Dick tests.

Number Tested	344
" Negative to Schick & Dick	107
" Positive to Schick & Dick	70
" Positive to Schick	107
" Positive to Dick	60
" Positive to Schick after 3 injections	30
" Positive to Dick after 5 injections	17

Fourteen of these required an additional 5th dose before becoming negative, while two required 2 additional injections before they were negative. One was allergic to the Dick test and to the control after she had received the five injections.

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DISCUSSION

DR. PASCAL F. LUCCHESI, (Superintendent, Philadelphia Hospital for Contagious Diseases) (By invitation): Mr. Chairman, Members of the Medical Society of Delaware, and Guests: I am both pleased and honored by your invitation to discuss Dr. Boines' paper and to share with you our experiences at the Philadelphia Hospital for Contagious Diseases, where we have conducted a similar program since 1926.

Immunization against diphtheria and scarlet fever is an important part of the routine program of protection offered the personnel of most contagious disease hospitals. Without the aid of these valuable agents, the personnel of isolation hospitals would spend many useless days confined to beds, requiring medical and nursing care, instead of dispensing this service to patients. But although the risk of contracting these diseases is greatest to doctors, nurses and attendants of contagious hospitals, there is nevertheless a greater risk to the personnel of large general hospitals. However, the most important thing to bear in mind is not that a doctor, nurse or attendant has developed a contagious disease, but the number of people exposed, the number of quarantine days imposed, and the financial loss both to the hospital and family.

During a ten-year period, 207 doctors and nurses have been sent to the Philadelphia Hospital for Contagious Diseases from thirty-one city hospitals, suffering from scarlet fever. Of this group, 196 were nurses and 11 were interns. The nursing group consisted of 170 students and 26 graduates. This professional group spent 6,545 sick days, or 17.9 years, in isolation. But, this is only part of the

story. Undoubtedly, many susceptible persons contracted scarlet fever from these exposures.

It is, therefore, a pleasure to note that Dr. Boines has begun a program in the city of Wilmington which will tend to eliminate this unnecessary waste of manpower. Today, more than ever, every hospital requires every medical and nursing day available. We cannot afford to waste in useless isolation a single precious minute of our professional groups' time, for there are only a limited number of doctors and nurses available to us.

I fully appreciate the vast amount of work and time involved in the testing of 344 persons for susceptibility to diphtheria and scarlet fever, and in immunizing the susceptible ones.

Our procedure is similar to that employed by Dr. Boines, except in the use of the Schick test. We use a control and read our tests three to five days later, whereas Dr. Boines does not use a control and reads his tests 72 hours later. Perhaps this explains the difference in susceptibility in our groups. Dr. Boines obtained 50% positive Schick tests in graduate nurses, 50% in student nurses, and 57% in the personnel, whereas we obtained 20.7% positive Schick tests in 58 doctors, 19.2% in 151 nurses, and 13.9% in 165 other employees. Some of this difference may be explained on the basis of susceptibility, since most of Dr. Boines' group came from rural areas, whereas most of our group are from urban sections. Nevertheless, I believe that the reading of the Schick test 3 or 5 days after performance, if no control is used, or 72 hours when control is used, would reduce his figures somewhat.

From 1926 to 1938, 1,010 doctors and nurses were tested; 249 or 24.7% were found susceptible, and immunized against scarlet fever. In this group 793 were nurses, of whom 161 or 20.3% were susceptible. Fifty-eight ill days were experienced by them as a result of the injections. Of the 217 doctors tested, 88 or 40.5% were found susceptible, and sixteen ill days were experienced.

Dr. Boines' group of 37.5% susceptibles is slightly higher than ours but, as explained above, this is probably due to the difference in susceptibility in the two groups.

In October, 1939, we started the intradermal method of scarlet fever immunization which is employed by Dr. Boines. Up to August, 1941, 387 were tested, of which 64 or 17.6% were found susceptible. The group consisted of 58 doctors, of whom 19 or 32.8% were positive; 148 nurses, 25 or 16.9% positive; 181 employees, 24 or 13.3% positive. Two weeks after the last dose 89.5% of the doctors, 70.8% of the nurses, and 100% of the employees were found immune. Those positive were given another dose and were found to be immune on re-testing. We have not had the opportunity of re-testing all of the group found immune or those immunized, since most of the doctors have returned to their hospitals and many of the nurses have left our employ; but we are in the process of re-testing those available at present. The results will be on hand at a future date.

I agree with the recommendations made by Dr. Boines, for the hospital personnel can only be kept free from contagion by carrying out a rigid immunization program.

DR. LEWIS B. FLINN (Wilmington): I would like to congratulate Dr. Boines on some of his work. I think all of us in Wilmington can be very proud of what he has done. I would like to ask just one question of Dr. Boines. It has been my impression that after being immunized there was somewhat of a latent period before the maximum immunity was obtained. It has been our custom, therefore, to test, re-test, re-check the immunization, not a week or two later, but some months later.

If I understand the discussion correctly, those individuals who were found to have positive Schick tests were tested shortly after the immunization was completed. How long is the optimum time for the re-Schicking? In ordinary practice I think most pediatricians have waited six months. That interval may have to be readjusted.

DR. T. E. HYNSON (Smyrna): I am very much interested in this method of immunization that Dr. Boines and Dr. Lucchesi have been speaking of because it looks to us as if it may be a step towards a practical method of wholesale immunization, which as yet is entirely out of the question. Because of the long course of injections necessary, five or more, and the reactions in public health, general

rural public health, immunization against scarlet fever is somewhat practicable, and it is entirely questionable whether an attempt at it is worth while. At this time, because of the relatively small number of severe cases we encounter and the relatively high immunity, we question whether it is a useful procedure, whether an attempt at wholesale immunization is a useful procedure. It unquestionably is in an institution, where there is a high rate of exposure.

But we are interested in any step towards a method by which the general population can be immunized, as we have already succeeded in doing with diphtheria.

Other than that, Dr. Boines, I think I haven't anything to add.

DR. BOINES: Dr. Lucchesi brought up an interesting point regarding susceptibility as between city and rural individuals. It has been known, of course, that the rural population is more susceptible to scarlet fever than city individuals who have to be in crowded places, and come in contact with all these infections.

Dr. Lucchesi's paper referred to nurses who have spent years in the large hospitals in Philadelphia and who have come in contact with some of those infections already, while ours are student nurses who come from small towns, practically all of them. If we can be bold enough to class Wilmington as a city, as I have done here, in 67 of the new group we are now doing, 26 are positive to the Dick, or 39 per cent, a smaller percentage than I had in the previous group. Of these, 13 are city people, or 50 per cent, and rural, 13, or 50 per cent, just half, positive to the Schick, 23, or 37 per cent. And again it is about 50-50 as to those who come from the city of Wilmington and those who come from the country.

Twenty-eight were negative to the Schick and Dick, or 42 per cent, of which 14 come from the city and 15 from the rural areas. So you see the difference there.

Dr. Lucchesi remarked about reading the tests before we do. That may be a source of error in not doing the control. In this new group I read all the tests in five days, so I think the error there of many positives may be much smaller. We didn't do a control because it takes quite a large amount of time and work. The results are known by workers who do a lot of work in this field, that those who are susceptible to the toxin will have the false reaction fade out in about two or three days, whereas the positive Schick remains a good test by the end of five days or longer.

Dr. Flinn brought up the question about the period in which the Schick test may become negative after the immunization. Of course when we deal with nurses in a hospital we like to test them and immunize them as soon as possible in order to get them back to work and contact with the patients, especially when they go to the contagious hospitals. As you noticed from my figures as well as those of Dr. Lucchesi, well over 80 per cent were negative two weeks after the last injection of diphtheria toxin-antitoxin, as well as the scarlet fever individuals, and only a small per cent of 15 or 20 were not negative after the two weeks, who required an additional injection. That meant waiting two more weeks before the testing became negative. So that we would say four weeks after the three tests are given for diphtheria, or five for scarlet fever, a maximum of four weeks after the last dose, most of the individuals are rendered negative.

Of course, probably it compares better than with toxoid. With toxoid there is a waiting period of six months before the Schick test becomes negative, but in these cases we did not use a toxoid.

As to Dr. Hynson's reference as to making this a public health measure only in recent years, the last year or two, the method has been used in general in immunizing not so much individuals but in groups and colleges, institutions where children are kept in homes, and so forth. The best results are obtained in immunizing contacts to scarlet fever patients, and that is done now in many cities and many localities. City Health Boards have taken up the matter, especially in Philadelphia, where they are trying it out, and I think it is working very well. As soon as scarlet fever is reported in a home the social worker goes to the home and takes all the contacts to the scarlet fever clinic and a Dick test is done. Those found positive to the Dick

(Concluded on Page 154)

Editorial

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OUR NEW ADDRESS

The editorial offices of the Delaware State Medical Journal have been removed, as of June 1st, from 1022 Du Pont Building, where they have been located for twenty-three years, to 618 Citizens Bank Building, where more commodious quarters are available. This is also the new mailing address of the business office. It is expected that the change will result in increased effectiveness in both departments. The former telephone number —Wilmington 2-6512—is retained.

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Thank you.

UNIFORM LICENSURE NEEDED

Immediate steps should be undertaken for the establishment of uniform standards of licensure of physicians, *The Journal of the American Medical Association* declares in its May 9 issue, pointing out that war conditions emphasize the great need for such uniformity. *The Journal* says:

"The results of the state licensing examinations published in this issue of *The Journal* are striking evidence of lack of uniformity of standards of licensure among the various states. Seven states reported not one failure in their 1941 licensing examinations; indeed, they had not had a failure in the past five years. Twelve additional states have reported failures of less than 1 per cent during the same period. Other states, notably New York, have each year reported a high percentage of failures.

"In New York 21.8 per cent of the graduates of the New York State medical colleges who tried the New York State licensing examinations failed, while 39.4 per cent of the graduates of other approved medical colleges in the United States who tried these same examinations failed. Of the 145 graduates of New York State medical colleges who tried licensing examinations in other states, four, or 2.8 per cent, failed.

"The lack of uniformity of results in some states is made more obvious by the fact that a candidate is passed if he receives an average of 75 per cent and is not below 50 per cent in any subject. Furthermore, in case of failure in not more than two subjects the applicant may be entitled to another examination in the subjects failed and is considered conditioned and is not reported as a failure.

"Paradoxically, New York, which reported the highest percentage of failures among the graduates of approved medical colleges on its own examinations, issued a greater number of licenses on the basis of credentials without examination than did any other state.

"In spite of this lack of uniformity, the

(*Concluded on Page 154*)

UNIFORM LICENSURE NEEDED

(*Concluded from Page 153*)

fact is striking that the graduates of the foreign medical schools and the unapproved schools in the United States showed the highest percentage of failures, 59.6 and 46.0 respectively. Six states licensed graduates of unapproved schools during 1941. Four states granted unlimited licenses to practice medicine to graduates of osteopathic schools.

"The best interests of the public and of the medical profession seem to demand serious thought right now on the establishment of uniform standards of licensure. These not only would facilitate the migration of qualified physicians from one state to another but would offer to the public greater assurance of the training and competence of practicing physicians. War conditions, involving as they do the migration of great masses of the population including physicians, emphasize the great need for such uniformity.

"Is it unreasonable to hope that all states will sometime be willing to maintain standards high enough to make such uniformity possible?"

Toxin Antitoxin Immunization and Intradermal Immunization Against Scarlet Fever in Adults

(*Concluded from Page 152*)

test are given a dose of scarlet fever antitoxin in order to protect them from the disease passively, and then they are immunized.

Of course, this is done on a voluntary basis. You can't force these people to be immunized, but after the seriousness of the disease is explained to them I am very sure there is very little objection on the part of the parents in having other children or adults in the same family protected from scarlet fever, since we all know the dangers and the complications and the high mortality resulting from scarlet fever.

FREEDOM IS MADE OF SIMPLE STUFF

HAZEL PARKER

From the archives of broken peace we are bringing out old words and dusting them off for use again as shining lanterns to lead us through the darkness of another war.

Words like freedom, justice and truth—all of them hard to define, none of them used more frequently than freedom.

You cannot say what freedom is, perhaps, in a single sentence. It is not necessary to define it. It is enough to point to it.

Freedom is a man lifting a gate latch at dusk and sitting for a while on the porch, smoking his pipe, before he goes to bed.

It is the violence of an argument outside an election poll; it is the righteous anger of the pulpits.

It is the warm laughter of a girl on a park bench.

It is the rush of a train over the continent and the unafraid faces of people looking out the windows.

It is all the howdys in the world, and all the hellos.

It is Westbrook Pegler telling Roosevelt how to raise his children; it is Roosevelt letting them raise themselves.

It is Lindbergh's appeasing voice raised above a thousand hisses.

It is Dorothy Thompson asking for war; it is General Hugh S. Johnson asking her to keep quiet.

It is you trying to remember the words to The Star-Spangled Banner.

Freedom—it is you.—*Louisville Courier-Journal.*

Intolerance to Diethylstilbestrol

Nausea and vomiting have been the most frequent side-effects following administration of stilbestrol (diethylstilbestrol). A recent report (J. A. M. A., 119:400, May 30, 1942) points out that there is a definite relation between these symptoms and the nausea and vomiting of early pregnancy. If one will merely take the time to ask the prospective patient if she had nausea and vomiting with a previous pregnancy, it would serve as a warning to give not over 0.25 mg. daily as an initial dose. Desensitization may be accomplished by giving 0.1 mg. tablets once daily for five days, then increasing the dose gradually until the therapeutic level is reached. Diethylstilbestrol, Lilly (formerly known as stilbestrol) is available in 0.1 mg. tablets, as well as in larger doses, for oral administration.

BOOK REVIEWS

Health Education of the Public. By W. W. Bauer, M. D., Director, Bureau of Health Education, A. M. A., and Thomas G. Hull, Ph. D., Director, Scientific Exhibit, A. M. A. 2nd Edition. Pp. 312, with 52 illustrations. Cloth. Price, $2.75. Philadelphia: W. B. Saunders Company, 1942.

This volume contains a complete description and evaluation of the various methods of getting to the public facts and figures concerning individual and community health. Apparently every worthwhile technique for doing this is included. The book abounds with practical advice, much of it of the "don't do" variety, a godsend to the novice. In no other volume can be found as complete and authoritative a text on this subject; the book should be in the hands of every person who attempts to conduct a campaign of health education of the public.

Synopsis of Materia Medica, Toxicology and Pharmacology. By Forest R. Davidson, M. B., Ph. D., formerly Assistant Professor of Pharmacology, University of Arkansas. Second edition. Pp. 695, with 45 illustrations. Cloth. Price, $5.75. St. Louis: C. V. Mosby Company, 1942.

This second edition, within two years, brings the text up to date, and despite numerous deletions, the important additions add some 60 pages to the previous total. The arrangement is the same as in the first edition. The style is not too terse, but this text is certainly meaty, and even though it is a synopsis, the author crowds in an exceptional amount of material per page. The work is authoritative, and we heartily recommend it.

The Kenny Method of Treatment for Infantile Paralysis. By Wallace H. Cole, M. D., Professor of Surgery; John F. Pohl, M. D., Clinical Instructor of Orthopedic Surgery, and Miland E. Knapp, M. D., Clinical Assistant Professor of Radiology; all of the University of Minnesota. Pp. 47. Price: gratis. New York: National Foundation for Infantile Paralysis, Inc., 1942.

This little brochure constitutes publication No. 40 of the N. F. I. P. The description of the Kenny technique is brief but impressive, and includes her ideas on symptomatology as well as on treatment. This is not a text book; it merely aims at clarifying what she has written about the technique. It will be of value to all who are interested in the Kenny method.

Schering Clinical Guides. Vol. 1—Female Follicular Hormone Therapy. 58 Pp. Vol. 2—Corpus Luteum Hormone Therapy. 47 Pp. Vol. 3—Male Sex Hormone Therapy. 52 Pp. Prepared and published by the Schering Medical Research Division, Schering Corporation, Bloomfield, N. J., 1942.

These brochures, while brief, are authoritative, and represent the boiled down essence of the 500 references they include. The charts are helpful, and the indices complete. Together, they represent an up-to-date summary of the subject. The sets come boxed, and any member of the medical profession can procure a set merely for the asking.

CORRECTION

In THE JOURNAL for May, 1942, page 136, appeared a review of "Synopsis of Ano-rectal Diseases," by Louis J. Hirschman, M. D., which stated that it "maintains the *syruptic* type." This, of course, should read *synoptic*. Our apologies to the author and to the Mosby Company.

PARTY FOR DEPARTING DOCTORS

The New Castle County Medical Society held an informal dinner dance on June 16th at the Shrine Club for the members of the Society, and their wives, who are leaving to serve with the armed forces. Cocktails were served at 6, the dinner followed at 7 and then dancing from 9.30 until 12.

Lt. Col. Victor D. Washburn acted as toastmaster, and responses were made by Dr. William Marshall, president of the Medical Society of Delaware; Dr. Willard F. Preston, president of the New Castle County Medical Society; and Mrs. Ervin M. Stambaugh, president of the Woman's Auxiliary of the M. S. of D. Rev. Hiram R. Bennett delivered the invocation and the benediction. Dr. George W. Vaughn was chairman of the committee in charge. The affair, arranged for on very short notice, was enjoyed by over 200 members, wives and guests.

DELAWARE DOCTORS IN THE SERVICES

(As complete and accurate as available information permits. Additions and corrections will be welcomed.)

Total (AMA Directory, 1940)	339	Active Duty	84 — 28.0%
Minimum over age 65	39	Awaiting Orders: Soon	6 — 2.0%
Maximum under age 65	300	Awaiting Orders: Indef.	9 — 3.0%
U. S. needs—Estimated as of 12-31-42		Retired	1 — 0.3%
32,000 out of 160,000, or 20%		Commissioned	101 — 33.3%

ARMY

Name	*City*	*Rank*
*Baker, John B.	Milford	Capt.
*Bancroft, Charles	Wilmington	1st Lt.
*Barsky, Joseph M.	Wilmington	Lt. Col.
Beatty, Gerald O.	Wilmington	Major
*Beck, Joseph R.	Dover	Capt.
*Berger, Simon M.	Selbyville	1st. Lt.
*Berlin, I. Irvin	Wilmington	1st Lt.
*Brown, Foster M.	Wilmington	Capt.
*Burton, Benjamin J.	Dover	Capt.
*Charamella, Italo	Wilmington	1st Lt.
*Cheff, Donald W.	Wilmington	1st. Lt.
*Clagett, A. H., Jr.	Milton	Capt.
*Comegys, Richard W.	Clayton	1st Lt.
*Connolly, George A.	Wilmington	1st Lt.
*D'Alonzo, C. A.	Wilmington	1st Lt.
*Davidson, D. T., Jr.	Wilmington	Capt.
*Davolos, Joseph J.	Wilmington	Capt.
*Dobson, Leslie M.	Lewes	1st Lt.
*Durham, J. Richard	Wilmington	1st Lt.
Ellis, Walter W.	Del. City	Col. (Ret.)
Everett, Franklin R.	Dover	Major
Feltz, Thomas	Wilmington	1st Lt.
*Flinn, Irvine M., Jr.	Wilmington	Major
Fenimore, William N.	Wilmington	1st Lt.
Ferguson, William R.	Wilmington	Capt.
*Fitchett, Lawrence L.	Milford	1st Lt.
*Gaumer, Herman E.	Wilmington	1st Lt.
*Gehret, Andrew M.	Wilmington	Capt.
*Giles, Junius A., Jr.	Wilmington	Capt.
*Gluckman, Albert G.	Wilmington	Capt.
*Gross, Benjamin A.	Wilmington	Capt.
*Harwitz, Morris	Wilmington	Capt.
Hazzard, William R.	Wilmington	Capt.
*Heather, Arthur J.	Wilmington	1st Lt.
*Homan, Frederic F.	Wilmington	1st Lt.
*Homan, James	Wilmington	1st Lt.
*Hudson, Floyd I.	Rehoboth	1st Lt.
*James, Oliver A.	Milford	1st Lt.
*Johnson, Wallace M.	Newark	Capt.
*Kelly, James	Wilmington	1st Lt.
*Kurland, Abram B.	Wilmington	1st Lt.
*Laird, Edmund G.	Wilmington	Major
*Lawrence, Chares T.	Wilmington	Capt.
*Lessey, Gerald	Wilmington	1st Lt.
*Lynch, John W.	Seaford	1st Lt.
*Maroney, John W.	Wilmington	Capt.
*Marvil, James E.	Laurel	Capt.
*Maske, Leslie I.	Wilmington	1st Lt.
*McDaniel, J. Stites, Jr.	Dover	1st Lt.
*McGuire, Harry T., Jr.	New Castle	Capt.
Mencher, Arthur A.	Newark	Capt.
Mercer, E. Harold	Dover	1st Lt.
*Moyer, Charles E.	Laurel	1st Lt.
*Munson, C. Leith	Wilmington	Major
*Murray, Roger M.	Wilmington	Capt.
*O'Donnell, Edward T.	Wilmington	Major
*Olivere, Peter J.	Wilmington	1st Lt.

*Active duty as of 6-30-42.

ARMY

Name	*City*	*Rank*
*Parvis, Edward S.	Wilmington	Capt.
*Pennington, Martin B.	Wilmington	1st Lt.
*Platt, David	Wilmington	1st Lt.
Poole, Gerald O.	Wilmington	Major
*Preston, Daniel J.	Wilmington	Capt.
Preston, Willard F.	Wilmington	Major
*Reardon, William T.	Wilmington	1st Lt.
*Rennie, Sylvester W.	Wilmington	Capt.
Resnick, Elton	Wilmington	1st Lt.
*Rovitti, Francis P.	Wilmington	1st Lt.
*Russo, Joseph R.	Wilmington	Capt.
*Schreader, Charles J.	Newark	1st Lt.
Scull, Carl B., Jr.	Dover	Capt.
*Shaw, Paul A.	Wilmington	Capt.
*Skura, Frank S.	Wilmington	1st Lt.
*Slovin, Isador	Wilmington	1st Lt.
*Smith, Alexander A.	Wilmington	Capt.
*Sortman, Harold P.	Wilmington	1st Lt.
*Stat, Sidney	Wilmington	Capt.
*Stradley, Shermer H., Jr.	Wilmington	1st Lt.
*Stroud, Henry E.	Seaford	1st Lt.
Szatkowski, Eugene J.	Wilmington	1st Lt.
*Taylor, Harry	Wilmington	1st Lt.
Thomas, Roger B.	Wilmington	1st Lt.
*Urie, J. William	Elmhurst	1st Lt.
*VanValkenburgh, Geo. M.	Georgetown	Capt.
*Walker, George L.	Wilmington	1st Lt.
*Warren, Robert O. Y.	Wilmington	Major
*Washburn, Victor D.	Wilmington	Lt. Col.

NAVY

Anderson, Lang W.	Wilmington	Lt. (SG)
*Borkowski, Charles P.	Wilmington	Lt. (JG)
*Bowdle, Frederick A.	Wilmington	Lt. (JG)
*Briggs, H. Ward	Wilmington	Lt. (SG)
*King, John W.	Wilmington	Lt. (JG)
*Martin John P.	Camden	Lt. (JG)
*Squires, Willard F., Jr.	Wilmington	Lt. (SG)

U. S. P. H. S.

Heck, A. Leon	Wilmington	Act. Asst. Surg.
*Tomlinson, Robert W.	Wilmington	Asst. Surg.
*Uhler, Claude	Wilmington	Asst. Surg.

VET. ADMIN.

*Latzo, John J.	Wilmington	

C. C. C.

*Riggin, George H.	Wilmington	

STATE GUARD

*Lynch, Raymond A.	Wilmington	Major
*Crutchley, Allan R.	Middletown	Capt.

*Active duty as of 6-30-42.